

CLAIM AMENDMENTS:

1. (Currently amended) A method of hyperthermally treating tissue in an animal, said method comprising the steps of:

introducing a temperature indicating substance into the bloodstream of said animal to flow through said tissue in a target site, said temperature indicating substance including a fluorescent dye encapsulated within a heat sensitive liposome, said fluorescent dye being releasable from said liposome at a temperature of about 45°C to about 49°C, and

applying a heat source to said target site and hyperthermally heating said tissue in said target site to at least 47°C to release said dye and to hyperthermally treat said tissue in said target site for a time sufficient to kill cells in said tissue substantially without denaturing proteins in said tissue, and fluorescing and visualizing said dye to indicate that a predetermined temperature has been attained at said target site.

Claim 2. (Cancelled)

Claim 3. (Cancelled)

4. (Previously presented) The method of claim 1, wherein said liposome encapsulates a bioactive compound, and said method comprises heating said liposome to release said bioactive compound.

5. (Previously presented) The method of claim 4, wherein said bioactive compound is heat activated.

6. (Original) The method of claim 4, wherein said bioactive compound is an antiproliferative agent or an antitumor agent.

7. (Previously presented) The method of claim 4, wherein said bioactive compound is selected from the group consisting of cisplatin, carboplatin, tetraplatin, iproplatin, adriamycin, mitomycin C, actinomycin, ansamitocin and bleomycin.

8. (Original) The method of claim 1, wherein said heat source is a laser source, a microwave source, an infrared source, or an ultrasonic source.

9. (Original) The method of claim 1, wherein said heat source is a heated fluid source, and where said method comprises applying said heated fluid to said target site.

10. (Currently amended) A method of detecting a threshold temperature and of hyperthermally treating tissue in an animal, said method comprising the steps of:

introducing a first fluorescent dye encapsulated in a first heat sensitive liposome into the bloodstream of an animal in a location to flow through a target site in said animal, said first fluorescent dye being releasable from said first heat sensitive liposome at a temperature of about 45°C to 49°C, and

heating said target site to a temperature to release said first fluorescent dye and fluorescing said first fluorescent dye to indicate and visualize a tissue temperature when said tissue reaches a temperature of at least 45°C, and continuing heating said target site for a time sufficient to hyperthermally treat said tissue and kill cells in said tissue and at a temperature below a protein denaturing temperature.

Claim 11. (Cancelled)

Claim 12. (Cancelled)

13. (Previously presented) The method of claim 10, comprising heating said target site to a temperature between about 47°C and about 49°C for about 1-10 minutes.

14. (Previously presented) The method of claim 10, wherein said first liposome encapsulates a bioactive compound, and wherein said method comprises heating said first liposome to release said bioactive compound.

15. (Previously presented) The method of claim 14, wherein said bioactive compound is heat activated.

16. (Original) The method of claim 14, wherein said bioactive compound is an antiproliferative agent or an antitumor agent.

17. (Original) The method of claim 14, wherein said bioactive agent is selected from the group consisting of cisplatin, carboplatin, tetraplatin, iproplatin, adriamycin, mitomycin C, actinomycin, ansamitocin and bleomycin.

18. (Original) The method of claim 10, wherein said heat source is a laser source, a microwave source, an infrared source or an ultrasonic source.

19. (Original) The method of claim 10, wherein said heat source is a source of heated fluid and said method comprises applying said heated fluid to said target site.

20. (Currently amended) The method of claim 10, further comprising the step of introducing a second fluorescent dye encapsulated in a second heat sensitive liposome into said bloodstream of said animal, said second fluorescent dye being releasable from said second liposome at a temperature of at least 50°C, and visualizing and detecting said second fluorescent dye released from said second liposomes and reducing said temperature of said tissue to a temperature below 50°C in response to said detected second dye.

21. (Original) The method of claim 20, wherein said second fluorescent dye is released from said second liposome at a temperature where protein denaturization occurs, and wherein said temperature of said tissue is reduced below the protein denaturization temperature in response to said detected second fluorescent dye.

22. (Original) The method of claim 20, comprising heating said tissue in said target site to a temperature below a protein denaturization temperature of said tissue and below said release temperature of said second fluorescent dye.

23. (Currently amended) A method of hyperthermally treating tissue of an animal, said method comprising the steps of:

introducing a temperature indicating substance into the bloodstream of said animal to flow through a target site, said temperature indicating substance including a first fluorescent dye encapsulated in a first temperature sensitive liposome, said first fluorescent dye being releasable from said first liposome by heating to a temperature of about 45°C to about 49°C, and ~~a~~ introducing a second fluorescent dye encapsulated in a second temperature sensitive liposome, said second fluorescent dye being releasable from said second liposome by heating to a temperature of at least 50°C, and

heating said target site and said first temperature sensitive liposome to a temperature sufficient to release said first liposome, and fluorescing said first fluorescent dye to indicate an effective temperature of at least 45°C for hyperthermally treating said tissue without releasing said second fluorescent dye from said second liposomes.

24. (Previously presented) The method of claim 23, comprising monitoring and detecting a fluorescence of said second fluorescent dye when released from said second temperature sensitive liposome and reducing said temperature of said tissue below a protein denaturing temperature of said tissue in response to a detection of said second fluorescent dye released from said second temperature sensitive liposome.

25. (Original) The method of claim 23, wherein said first fluorescent dye fluoresces a color different from a color of said second fluorescent dye.

26. (Original) The method of claim 23, wherein said first liposome comprises a phospholipid selected from the group consisting of dipalmitoylphosphatidyl-choline, dipalmitoylphosphatidyl-glycerol, and mixtures thereof.

27. (Previously presented) The method of claim 23, wherein said first liposome comprises a C₁₇₋₁₉phosphatidyl-choline, wherein said second liposome releases said second fluorescent dye at a temperature of about 48°C to 49°C.

28. (Currently amended) The A method of claim 23, hyperthermally treating tissue of an animal, said method comprising the steps of:

introducing a temperature indicating substance into the bloodstream of said to flow through a target site, said temperature indicating substance including a first fluorescent dye encapsulated in a first temperature sensitive liposome, said first fluorescent dye being releasable from said first liposome by heating to a temperature of about 45°C to about 49°C, and introducing a second fluorescent encapsulated in a second temperature sensitive liposome, said second fluorescent dye being releasable from said second liposome by heating to a temperature of at least 50 C, wherein said first liposomes encapsulate a bioactive compound, and

heating said target site and said first temperature sensitive liposome to a temperature sufficient to release said first liposome, and fluorescing said first fluorescent dye to indicate an effective temperature of at least 45°C for hyperthermally treating said tissue without releasing said second fluorescent dye from said second liposomes.

29. (Original) The method of claim 28, wherein said bioactive compound is selected from the group consisting of anti-proliferative agents and anti-tumor agents.

30. (Original) The method of claim 28, wherein said bioactive compound is cis-platin.

31. (Original) The method of claim 28, wherein said bioactive compound is a photoactivated compound, and wherein said method comprises activating said photoactivated compound to kill or inhibit multiplication of cells in said target site.

32. (Previously presented) The method of claim 23, wherein said tissue is heated to a temperature of about 47°C to about 49°C.

Claim 33. (Cancelled)

34. (Original) The method of claim 23, wherein said second temperature sensitive liposomes leak or rupture at a temperature of about 50°C to 60°C.

35. (Previously presented) The method of claim 1, further comprising heating said target site to a temperature of about 47°C to about 49°C.

36. (Previously presented) The method of claim 1, further comprising the step of introducing a second liposome containing a second fluorescent dye into the bloodstream of said animal to flow through said target site, wherein said liposome releases said dye at a temperature of about 50°C to about 60°C, and

monitoring release of said second dye from said second liposomes and reducing the temperature of said tissue in said target site to 49°C or less in response to a detection of said second dye released from said second liposomes.

37. (Previously presented) The method of claim 1, wherein said target site is in the eye.

38. (Previously presented) The method of claim 23, wherein said target site is in the eye.

39. (Previously presented) The method of claim 23, wherein said tissue in said target site is heated to a temperature below the temperature where said second dye is released from said second temperature sensitive liposome.

40. (Previously presented) The method of claim 23, further comprising monitoring and detecting release of said second fluorescent dye from said second heat sensitive liposome by fluorescing said second fluorescent dye, and

reducing the temperature of said tissue in said target site when release of said second fluorescent dye is detected.